while the fucose and/or bisect restrict the motion of 1-6 arm, shifting conformational equilibria. This is attributed to the change in the local hydrogen bond network around introduced Fuc/GlcNAc. This modulation mechanism helps to understand the affinity regulation of glycan binding to lectin.

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Molecular Modeling of Folding in Lactam-Modified (Glutamate + Lysine Analog) Conotoxins

Christopher R. DeLaney, Brittany A. Kovacs, **Pedro L. Muíño**.
Saint Francis University, Loretto, PA, USA.

We report a method to model the conformational folding of α-conotoxins and the factors that affect the synthesis of specific regioisomers by using a combination of molecular dynamics methods to determine the geometric factors (S-S distances and C-N distances in lactam-modified α-conotoxins) and *ab initio* methods to determine the conformational energy and molecular orbital information. In the literature, the replacement of the Cys2-Cys7 disulfide bridge with a lactam bridge causes a complete loss of activity. However, exchanging the larger Cys3-Cys13 bridge leads to analogues that exhibit considerable affinities for the receptor sites. In previous work [Osysko *et al*. *Biophys. J.* **2011**, *100*, 155a], we studied the effect of side-chain length at position 13 by replacing this amino acid with modified lysines, where one to four methylene units would separate the alpha carbon and the ammonium group. Cys 3 was then replaced by aspartate. In this work, we examine a similar effect but replacing Cys3 with a glutamate residue instead. The results show that thermal fluctuations lead to configurations where a molecular orbital overlap between S-S atoms (Cys2-Cys7) can take place, leading to the proper regioisomer formation. Furthermore, *ab initio* methods predict adequate orbital overlap between the sulfur atoms. The length of the methylene chain of the basic amino acid at position 13 affects the probability of forming a lactam bridge between positions 7 and 13. Surprisingly, we find that the best overlap conditions are achieved for very short chains (only one methylene group separating the amino group and the alpha carbon) and, to a slightly smaller extent, for the longest chains (four methylene groups, i.e. lysine). Few overlap arrangements were observed in the simulations with two or three methylene groups.